

### **REMARKS**

This is in response to the Office Action mailed October 3, 2001, in the above-referenced application. Applicants note with appreciation the courtesies extended to their undersigned representative, Melissa B. Pendleton, during the telephone interview of March 14, 2002. The substance of the discussion is incorporated in the following remarks.

Claim 1 is objected to as lacking proper antecedent basis. Claim 1 is amended to provide consistency throughout with regard to reference to the term "calcium triphosphate." Claims 24 and 27 are similarly amended.

Claims 1-3, 5, 6, 12-15, 21-35, and 38 are rejected under 35 USC § 112, first and second paragraphs. In particular, the Examiner objects to the use of the term "substantially." As discussed during the telephone interview, and without prejudice or disclaimer to Applicants, the term "substantially" is removed from independent claims 1, 13, 24 and 27. Applicants accordingly respectfully request withdrawal of these rejections.

Claims 1-3, 5, 6, 12-15, 21-35 and 38 are rejected under 35 USC § 102(a) or 102(b) as anticipated by, or alternatively, under 35 USC § 103 as obvious over WO 94/26872 to Davies. Applicants respectfully traverse this rejection.

The Davies publication is directed to the application of a sol-gel to a substrate, such as a quartz substrate, among others. The Office argues that during sintering, silicon from the quartz would permeate into the sol. Following the Davies procedure, however, the resultant film includes a gradient of silicon, such that the film includes areas with different concentration of silicon at different locations therein.

In contrast, in the invention, the hydroxyapatite precursor material is uniformly doped with stabilizing entities and thereafter the uniformly doped hydroxyapatite is sintered. The resultant tricalcium phosphate composition includes stabilizing entities uniformly distributed throughout, as recited in Claim 1. The Interview Summary dated March 18, 2002, indicates that removing the term "substantially" from the claims would support this argument. As noted above, independent claims 1, 13, 24, and 27 are so amended.

The structural differences between the composition of Claim 1 and the Davies product is illustrated in Figures 5a, 5b, and 5c of the present application. Figures 5a, 5b, and 5c present analytical data on the concentrations of the film components, including silicon, at different locations of a film prepared by sintering hydroxyapatite on a quartz substrate. See page 17, lines 5-11. The figures demonstrate that the resultant film includes a gradient of silicon, with areas of different silicon concentrations at different locations within the film.

In summary, the stabilizing entities are distributed uniformly throughout the tricalcium phosphate of the claimed invention. Thus the claimed composition differs from Davies. The claimed process is also different because the hydroxyapatite is uniformly doped with stabilizing entities prior to sintering, which is not taught by Davies. In addition, there is no motivation to modify the Davies process to provide the claimed invention. Davies does not recognize silicon as a stabilizing entity. Davies certainly does not teach or suggest proactively doping hydroxyapatite to uniformly distribute any stabilizing entity therein. Applicants accordingly respectfully request withdrawal of this rejection.

Claims 1-3, 12-14, 19, 22, 23, 31 and 34 are rejected under 35 USC § 102(b) as anticipated by U.S. Patent No. 5,232,878 to Kasuga et al. Applicants respectfully traverse this rejection as well.

The Kasuga et al. patent is also directed to a process that is very different from the claimed process. As a result, the end product of Kasuga et al. also differs structurally from the claimed product.

In particular, Kasuga et al. is directed to two processes for creating an inorganic biomaterial. Regardless of which of the two processes is employed, the resultant biomaterial includes sintered glass within a sintered stabilized zirconium matrix. The zirconium is not distributed within the sintered glass at all, much less uniformly distributed throughout the stabilized glass.

This can be seen by the discussion in Kasuga et al. at column 3, lines 3-37 (describing the first process) and column 3, lines 41-60 (describing the second process). In the first process, glass raw materials are melted and cooled to form a glass. The glass is then heated so as to precipitate a crystal of apatite and at least one crystal of alkaline earth metal silicate. The precipitated glass material is then mixed with partially stabilized zirconium and/or alumina powder and the mixture is heated to sinter the zirconium and/or alumina powder. As discussed in column 5, lines 43-45, the fully crystallized glass from step 1 of this process "cannot be sintered anymore." Column 5, lines 50-51 further states that in this first process, it is preferable "that the glass is crystallized so fully as to not be sintered again."

The second process described in the Kasuga et al. patent includes sintering calcium phosphate to form a calcium phosphate crystal sintered body, grinding the sintered body and thereafter adding stabilized zirconium powder and/or alumina powder, and lastly molding the mixture and heating to sinter the zirconium and/or alumina powder.

In both processes, Kasuga et al. do not concurrently sinter hydroxyapatite doped with stabilizing entities to provide tricalcium phosphate with stabilizing entities distributed therein, much less a uniform distribution of such entities. Rather, Kasuga et al. describe a sequential sintering process in which a first material is sintered (without subsequent sintering thereof) and zirconium materials are thereafter sintered in a separate step. As a result, the zirconium and/or alumina forms a framework surrounding but not distributed within the first sintered body.

Kasuga et al. is clearly distinguishable from the processes of independent Claims 13 and 19. Both claims 13 and 19 recite the step of uniformly doping the precursor materials with stabilizing entities prior to sintering and thereafter sintering the uniformly doped hydroxyapatite. Claim 19 is even further removed from Kasuga et al. because of the recitation therein that the silicon entities are provided in solution. Kasuga et al. nowhere teach or suggest the use of silicon, and further does not teach or suggest a solution of zirconium and/or aluminum particles.

Not only are the processes different, the resultant products are structurally distinguishable as well. As noted above, the Kasuga et al. process results in a glass embedded in a matrix of

zirconium. The zirconium is not distributed at all within the glass, and certainly is not uniformly distributed through the glass. In contrast, in Claim 1, the bioactive material includes stabilizing entities distributed uniformly throughout. Accordingly, in view of the foregoing, Applicants respectfully request withdrawal of this rejection as well.

Claims 1-3, 5, 6, 12-14, 21, 23, 24 and 31-34 are rejected under 35 USC § 102(b) as anticipated by U.S. Patent No. 4,983,182 to Kijima et al. Applicants respectfully traverse this rejection as well.

With regard to the pending claims, Applicants reiterate the arguments presented in the response filed concurrently with the filing of this RCE application. In addition, new claims 39-46 are added to specifically recite stabilizing entities useful in the invention. New claims 39-46 correspond to pending claims 1, 13, 24, 27, 31, 33, 34, and 35, respectively, but for the added Markush language from Claim 5, excluding zirconium as one of the entities. Applicants note with appreciation the suggestion by the Examiner to use a Markush group to list the stabilizing entities. For this reason alone, the new claims are patentable over the Kijima et al. patent.

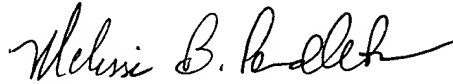
The rejections of record having been addressed in full in the foregoing, Applicants respectfully submit that this application is now in condition for allowance, which action is respectfully solicited. Should the Examiner have any questions regarding the foregoing, it is respectfully requested that he contact the undersigned at his convenience to expedite examination.

It is not believed that extensions of time or fees for net addition of claims are required, beyond those that may otherwise be provided for in documents accompanying this paper. However, in the event that additional extensions of time are necessary to allow consideration of this paper, such extensions are hereby petitioned under 37 CFR § 1.136(a), and any fee required

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Filed: June 29, 1998  
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therefore (including fees for net addition of claims) is hereby authorized to be charged to Deposit Account No. 16-0605.

Respectfully submitted,



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Grace R. Rippey

**Version with Markings to Show Changes Made:**

1. (Three times amended) A bioactive artificial sintered composition for consistently supporting bone cell activity, said composition comprising [substantially] uniformly stabilized tricalcium phosphate having stabilizing entities distributed [substantially] uniformly throughout, wherein said uniformly stabilized tricalcium phosphate is insoluble in physiological fluids.

13. (Three times amended) A process for stabilizing an artificial sintered composition of tricalcium phosphate phases having a morphology suitable for supporting bone cell activity, said process comprising [substantially] uniformly doping a hydroxyapatite substance with stabilizing entities and sintering said [substantially] uniformly doped hydroxyapatite substance; wherein sintering converts said [substantially] uniformly doped hydroxyapatite substance into primarily uniformly stabilized [alpha] tricalcium phosphate which is insoluble in physiological fluids and said stabilizing entities stabilize the formed [alpha] tricalcium phosphate within the phosphate phases.

24. (Twice amended) A sintered artificial microporous polycrystalline structure for supporting bone cell activity, said structure comprising sintered [substantially] uniformly stabilized tricalcium phosphate phases having a globular surface morphology of loosely interconnected rounded granules with interconnected micropores in said structure, wherein said [substantially] uniformly stabilized tricalcium phosphate phases are developed by the conversion of a hydroxyapatite substance [substantially] uniformly doped with stabilizing entities at sintering temperatures into stabilized tricalcium phosphate phases, wherein said [substantially] uniformly stabilized [alpha] tricalcium phosphate is insoluble in physiological fluids.

27. (Twice amended) An implantable calcified bone matrix comprising:

- a) a structure for supporting said matrix;
- b) a layer of [substantially] uniformly stabilized tricalcium phosphate phases developed by the conversion of a hydroxyapatite substance [substantially] uniformly doped with stabilizing entities at sintering temperatures into [substantially] uniformly stabilized tricalcium phosphate where said stabilizing entities insolubilize and stabilize the tricalcium phosphate phases;
- c) a boundary layer deposited by osteoblasts cultured on said layer of stabilized tricalcium phosphate phases; and
- d) a mineralizing collagenous matrix secreted by such cultured osteoblasts.